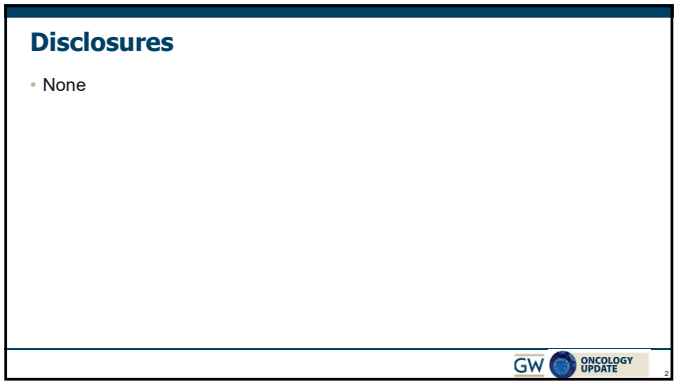
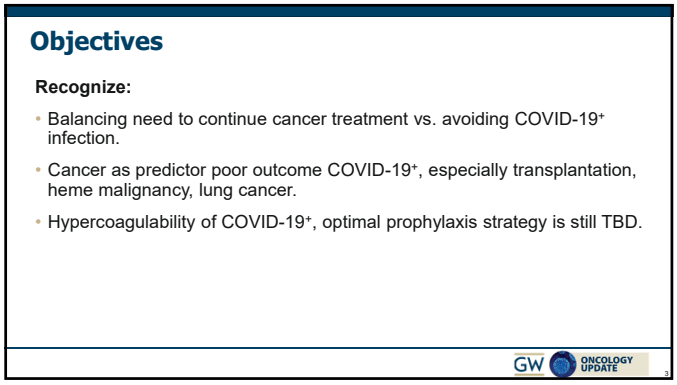




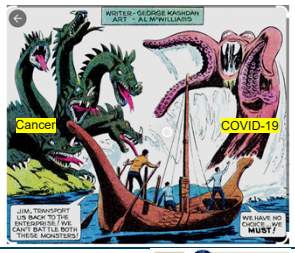
PERSPECTIVE

BETWEEN SCYLLA AND CHARYBDIS

Between Scylla and Charybdis — Oncologic Decision Making in the Time of Covid-19

"For on one side lay Scylla and on the other divine Charybdis"

Homer, *The Odyssey*, Book 4



Lewis. *NEJM*. 11 Jun 2021; 382:24.

GW ONCOLOGY UPDATE 4

Presenting Sxs of COVID-19 are the same in Cancer Patients

	Guan *et al.*, NEJM n = 1099	Wang *et al.*, JAMA n = 138	Zhou *et al.*, Lancet n = 191
most common sxs	cough (68%) fever (44%) fatigue (38%) sputum (34%) SOB (19%)	fever (99%) fatigue (70%) cough (59%) anorexia (40%) myalgia (35%)	fever (94%) cough (79%) SOB (29%) fatigue (23%) sputum (23%)

Guan, *et al. NEJM*. 2020;382:1708-1720. Wang, *et al. JAMA*. 2004;323 (11):1061-1069. Zhou, *et al. Lancet*. 2020;395:1054-1062.

GW ONCOLOGY UPDATE 5

Are Cancer Patients more likely to get/have COVID-19? YES

	Guan *et al.*, NEJM n = 1099	Wang *et al.*, JAMA n = 138	Zhou *et al.*, Lancet n = 191
co-morbidity	HTN (15%) DM (7%) CAD (3%) hep B (2%)	HTN (31%) CAD (15%) DM (10%) cancer (7%)	HTN (30%) DM (19%) CAD (8%) COPD (3%)

Guan, *et al. NEJM*. 2020;382:1708-1720. Wang, *et al. JAMA*. 2004;323 (11):1061-1069. Zhou, *et al. Lancet*. 2020;395:1054-1062.

GW ONCOLOGY UPDATE 6

Are Cancer Patients more likely to get/have COVID-19? YES

JAMA Oncology | Original Investigation

Analyses of Risk, Racial Disparity, and Outcomes Among US Patients With Cancer and COVID-19 Infection

QuanQiu Wang, MS; Nathan A. Berger, MD; Rong Xu, PhD

PARTICIPANTS This retrospective case-control analysis of patient electronic health records included 73.4 million patients from 360 hospitals and 317 000 clinicians across 50 US states to August 14, 2020. The odds of COVID-19 infections for 13 common cancer types and adverse outcomes were assessed.

Those with recent cancer diagnosis were at significantly increased risk for COVID-19 infection (aOR, 7.14 [95% CI, 6.91-7.39]; $P < .001$), with the strongest association for recently diagnosed leukemia (aOR, 12.16 [95% CI, 11.03-13.40]; $P < .001$), non–Hodgkin lymphoma (aOR, 8.54 [95% CI, 7.80-9.36]; $P < .001$), and lung cancer (aOR, 7.66 [95% CI, 7.07-8.29]; $P < .001$) .

Patients with cancer and COVID-19 had significantly worse outcomes (hospitalization, 47.46%; death, 14.93%) than patients with COVID-19 without cancer (hospitalization, 24.26%; death, 5.26%) ($P < .001$) and patients with cancer without COVID-19 (hospitalization, 12.39%; death, 4.03%) ($P < .001$).

Wang *et al. JAMA Oncology.* 2021; 7:220-227.

GW ONCOLOGY UPDATE 7

Poor Outcome of COVID-19+ Cancer patients

Article

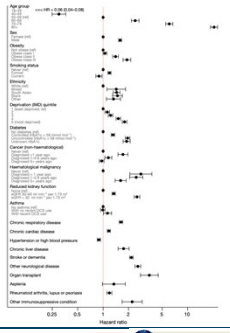
nature

Factors associated with COVID-19-related death using OpenSAFELY

Elizabeth J. Williamson[1*], Alex J. Walker[1*], Krishnan Bhaskaran[1*], Seb Bacon[2,3], Chris Bates[1,4], Caroline E. Morton[1], Helen J. Curtis[1], Amir Mehrkar[1], David Evans[1], Peter Inglesby[1], Jonathan Cockburn[1], Helen I. McDonald[1,5], Brian MacKenna[1], Laurie Tomlinson[1], Ian J. Douglas[1], Christopher T. Rentsch[1], Rohini Mathur[1], Angel Y. S. Wong[1], Richard Grieve[1], David Harrison[6], Harriet Forbes[1], Anna Schultze[1], Richard Croker[1], John Parry[7], Frank Hester[8], Sam Harper[9], Rafael Perera[8], Stephen J. W. Evans[1], Liam Smeeth[1,4] & Ben Goldacre[2,10]

n = NHS data base of 10,926 COVID-19-related deaths

Fig. 3 | Estimated hazard ratios for each patient characteristic from a multivariable Cox model. Hazard ratios are shown on a log scale. Error bars represent the limits of the 95% confidence interval for the hazard ratio. IMD, index of multiple deprivation; obese class I, BMI 30–34.9; obese class II, BMI 35–39.9; obese class III, BMI ≥ 40; OCS, oral corticosteroid; ref, reference group. All hazard ratios are adjusted for all other factors listed other than ethnicity. Ethnicity estimates are from a separate model among those individuals for whom complete ethnicity data were available, and are fully adjusted for other covariates. Total $n = 17,278,392$ for the non-ethnicity models, and 12,718,279 for the ethnicity model.



Williamson *et al. Nature.* 20 Aug 2020; 584:430-436.

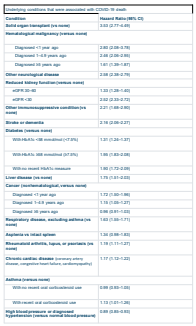
GW ONCOLOGY UPDATE 8

Cancer on CDC list of comorbidities as Risk Factors for Severe COVID-19

Centers for Disease Control and Prevention. Underlying medical conditions associated with high risk for severe COVID-19: Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

See especially:

- Solid organ transplant
- Hematologic malignancies
- Lung cancer



Williamson *et al. Nature.* 20 Aug 2020; 584:430-436.

GW ONCOLOGY UPDATE 9

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study

Nicole M Kuderer*, Toni K Choueiri*, Dimpy P Shah*, Yu Shyr*, Samuel M Rubinstein, Donna R Rivera, Sanjay Shete, Chih-Yuan Hsu, Aakash Desai, Gilberto de Lima Lopes Jr, Petros Grivas, Corrie A Painter, Solange Peters, Michael A Thompson, Ziad Bakouny, Gerald Batist, Tanios Bekaii-Saab, Mehmet A Bilen, Nathaniel Bouganim, Mateo Bover Larroya, Daniel Castellano, Salvatore A Del Prete, Deborah B Doroshow, Pamela C Egan, Arielle Elkrief, Dimitrios Farmakiotis, Daniel Flora, Matthew D Galsky, Michael J Glover, Elizabeth A Griffiths, Anthony P Gulati, Shilpa Gupta, Navid Hafez, Thorvardur R Halfdanarson, Jessica E Hawley, Emily Hsu, Anup Kasi, Ali R Khaki, Christopher A Lemmon, Colleen Lewis, Barbara Logan, Tyler Masters, Rana R McKay, Ruben A Mesa, Alicia K Morgans, Mary F Mulcahy, Orestis A Panagiotou, Prakash Peddi, Nathan A Pennell, Kerry Reynolds, Lane R Rosen, Rachel Rosovsky, Mary Salazar, Andrew Schmidt, Sumit A Shah, Justin A Shaya, John Steinharter, Keith E Stockerl-Goldstein, Suki Subbiah, Donald C Vinh, Firas H Wehbe, Lisa B Weissmann, Julie Tsu-Yu Wu, Elizabeth Wulff-Burchfield, Zhuoer Xie, Albert Yeh, Peter P Yu, Alice Y Zhou, Leyre Zubiri, Sanjay Mishra, Gary H Lyman*, Brian I Rini*, Jeremy L Warner*, on behalf of the COVID-19 and Cancer Consortium

UK Coronavirus Cancer Monitoring Project (UKCCMP)

COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study

Lennard YW Lee*, Jean-Baptiste Cazier*, Vasileios Angelis, Roland Arnold, Vartika Bisht, Naomi A Campton, Julia Chackathayil, Vinton WT Cheng, Helen M Curley, Matthew W Fittall, Luke Freeman-Mills, Spyridon Gennatas, Anshita Goel, Simon Hartley, Daniel J Hughes, David Kerr, Alvin JX Lee, Rebecca J Lee, Sophie E McGrath, Christopher P Middleton, Nirupa Murugaesu, Thomas Newsom-Davis, Alicia FC Okines, Anna C Olsson-Brown, Claire Palles, Yi Pan, Ruth Pettengell, Thomas Powles, Emily A Protheroe, Karin Purshouse, Archana Sharma-Oates, Shivan Sivakumar, Ashley J Smith, Thomas Starkey, Chris D Turnbull, Csilla Várnai, Nadia Yousaf, The UK Coronavirus Monitoring Project Team, Rachel Kerr†, Gary Middleton†

Kuderer, *et al.*. *Lancet*. 20 June 2020;395:1907-1918. Lee, *et al.*. *Lancet*. 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 10

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

Cohort study

Mar 2020 – Apr 2020

USA, Canada, Spain; age 56-76

Cancer patients new dx COVID-19+ (n = 928)

Assessed 30-day all-cause mortality

UK Coronavirus Cancer Monitoring Project (UKCCMP)

Prospective Observational study

Mar 2020 – Apr 2020

United Kingdom; age 59-76

Cancer patients new dx COVID-19+ (n = 800)

Assessed all-cause mortality or hospital d/c

Kuderer, *et al.*. *Lancet*. 20 June 2020;395:1907-1918. Lee, *et al.*. *Lancet*. 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 11

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

Type of malignancy§	
Solid tumours	758 (82%)
Breast	191 (21%)
Prostate	152 (16%)
Gastrointestinal	108 (12%)
Thoracic	91 (10%)
Gynaecological	49 (5%)
Renal cell carcinoma	45 (5%)
Endocrine	39 (4%)
Melanoma	38 (4%)
Head and neck	30 (3%)
Sarcoma	24 (3%)
Nervous system	12 (1%)
Solid tumour, not otherwise specified	43 (5%)
Haematological malignancies	204 (22%)
Lymphoid neoplasms	102 (11%)
Low-grade non-Hodgkin lymphoma	54 (6%)
High-grade non-Hodgkin lymphoma	27 (3%)
Acute lymphoblastic leukaemia	6 (1%)
Multiple myeloma	55 (6%)
Myeloid neoplasms	42 (5%)
Acute myeloid leukaemia	13 (1%)
Haematological malignancy, not otherwise specified	6 (1%)

UK Coronavirus Cancer Monitoring Project (UKCCMP)

Cancer type		
Lip, oral cavity, and pharynx	27 (3%)	4 (2%)
Digestive organs	150 (19%)	42 (19%)
Respiratory and intrathoracic organs	90 (11%)	32 (14%)
Melanoma (skin)	27 (3%)	4 (2%)
Breast	102 (13%)	18 (8%)
Female genital organs	45 (6%)	5 (2%)
Male genital organs	78 (10%)	30 (13%)
Urinary tract	50 (6%)	16 (7%)
Central nervous system	15 (2%)	3 (1%)
Lymphoma	60 (8%)	20 (9%)
Other haematological	109 (14%)	40 (18%)
Other or unspecified‡	47 (6%)	12 (5%)

Kuderer, *et al.*. *Lancet*. 20 June 2020;395:1907-1918. Lee, *et al.*. *Lancet*. 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 12

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

Cancer status†		
Remission or no evidence of disease	422 (45%)	
Present, stable, or responding to treatment	294 (32%)	
Present, progressive disease	102 (11%)	
Unknown	59 (6%)	
Data missing	51 (5%)	
Type of anticancer therapy§		
None in the 4 weeks before COVID-19 diagnosis	553 (60%)	
Non-cytotoxic therapy	206 (22%)	
Targeted therapy	75 (8%)	
Endocrine	85 (9%)	
Immunotherapy¶	38 (4%)	
Radiotherapy	12 (1%)	
Surgery‖	2 (<1%)	
Cytotoxic systemic therapy	160 (17%)	
Unknown	9 (1%)	
Recent surgery†		
None in the 4 weeks before COVID-19 diagnosis	811 (87%)	
Yes‖	32 (3%)	
Unknown	42 (5%)	
Data missing	43 (5%)	

UK Coronavirus Cancer Monitoring Project (UKCCMP)

Cancer stage		
Primary tumour localised	149 (19%)	40
Primary tumour locally advanced	78 (10%)	14
Metastatic	347 (43%)	103
Remission	21 (3%)	3
No information	205 (25%)	66
Cancer treatment within 4 weeks of COVID-19 diagnosis		
Chemotherapy	281 (35%)	75
Hormone therapy	64 (8%)	21
Immunotherapy	44 (6%)	10
Radiotherapy	76 (10%)	18
Surgery	29 (4%)	7
Targeted treatment	72 (9%)	16
Other§	60 (8%)	13
None	272 (34%)	92
No information	10 (1%)	1

Kuderer, *et al.. Lancet.* 20 June 2020;395:1907-1918. Lee, *et al.. Lancet.* 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 13

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

	Bivariable odds ratio	Multivariable partially adjusted odds ratio*
Age, per 10 years†	1·88 (1·58–2·24)	1·84 (1·53–2·21)
Sex		
Female	1 (ref)	1 (ref)
Male	1·94 (1·30–2·88)	1·63 (1·07–2·48)
Number of comorbidities		
0	1 (ref)§	1 (ref)§
1	3·12 (0·87–11·19)	1·87 (0·51–6·85)
2	9·52 (2·89–31·40)	4·59 (1·33–15·78)
3	13·54 (3·37–39·53)	5·04 (1·42–17·93)
≥4	8·77 (2·62–29·29)	3·55 (1·03–12·30)
Unknown	12·33 (2·71–56·01)	6·77 (1·42–32·33)
ECOG performance status		
0 or 1	1 (ref)	1 (ref)
2	4·84 (2·75–8·52)	3·89 (2·11–7·18)
3 or 4	7·33 (3·83–14·01)	5·66 (2·79–11·47)
Unknown	1·59 (0·93–2·73)	1·43 (0·81–2·50)
Cancer status		
Remission or no evidence of disease	1 (ref)	1 (ref)
Present, stable, or responding to treatment	1·57 (0·98–2·49)	1·79 (1·09–2·95)
Present, progressive disease	3·07 (1·77–5·33)	5·20 (2·77–9·77)
Other or unknown	2·24 (1·06–4·71)	2·71 (1·21–6·09)

UK Coronavirus Cancer Monitoring Project (UKCCMP)

	Odds ratio (95% CI)	p value	Adjusted p value
Sex	1·67 (1·19–2·34)	0·003	0·006
Age	9·42 (6·56–10·02)	<0·0001	<0·0001
Comorbidities			
Cardiovascular disease	2·32 (1·47–3·64)	0·0003	0·0019
Chronic obstructive pulmonary disease	1·80 (1·00–3·27)	0·063	0·375
Diabetes	1·61 (1·03–2·48)	0·032	0·190
Hypertension	1·95 (1·36–2·80)	0·0003	0·0015
Cancer stage			
Primary tumour localised	1·04 (0·67–1·64)	0·912	1·000
Primary tumour locally advanced	0·58 (0·29–1·09)	0·111	0·442
Metastatic	1·34 (0·90–2·01)	0·145	0·579
Remission	0·42 (0·10–1·43)	0·204	0·815

Kuderer, *et al.. Lancet.* 20 June 2020;395:1907-1918. Lee, *et al.. Lancet.* 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 14

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

Type of malignancy		
Solid tumour	1 (ref)	1 (ref)
Haematological malignancy	1·28 (0·78–2·09)	1·40 (0·83–2·37)
Multiple cancers	1·86 (1·09–3·17)	1·34 (0·77–2·34)
Type of anticancer therapy		
None in the 4 weeks before COVID-19 diagnosis	1 (ref)	1 (ref)
Non-cytotoxic therapy	0·80 (0·49–1·32)	1·04 (0·62–1·76)
Cytotoxic systemic therapy	1·02 (0·61–1·69)	1·47 (0·84–2·56)
Unknown	0·80 (0·10–6·46)	1·60 (0·18–14·14)
Recent surgery¶		
None in the 4 weeks before COVID-19 diagnosis	1 (ref)	1 (ref)
Yes	1·50 (0·60–3·74)	1·52 (0·58–3·96)
Unknown	0·66 (0·23–1·89)	0·78 (0·26–2·33)

UK Coronavirus Cancer Monitoring Project (UKCCMP)

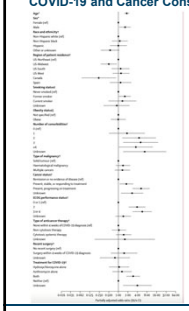
Cancer type			
Lip, oral cavity, and pharynx	0·42 (0·13–1·21)	0·116	1·000
Digestive organs	0·91 (0·60–1·38)	0·680	1·000
Respiratory and intrathoracic organs	1·50 (0·91–2·45)	0·121	1·000
Melanoma (skin)	0·37 (0·12–1·14)	0·079	1·000
Breast	0·48 (0·28–0·84)	0·009	0·141
Female genital organs	0·31 (0·11–0·81)	0·010	0·148
Male genital organs	1·99 (1·14–3·48)	0·015	0·230
Urinary tract	1·10 (0·58–2·12)	0·745	1·000
Central nervous system	0·64 (0·15–2·32)	0·760	1·000
Lymphoma	1·30 (0·75–2·30)	0·373	1·000
Other haematological	1·57 (1·01–2·42)	0·049	1·000
Cancer treatment within 4 weeks of COVID-19 diagnosis			
Chemotherapy	0·78 (0·55–1·11)	0·173	1·000
Hormone therapy	1·16 (0·64–2·06)	0·659	1·000
Immunotherapy	0·60 (0·27–1·24)	0·179	1·000
Radiotherapy	0·66 (0·37–1·17)	0·178	1·000
Surgery	0·83 (0·32–2·15)	0·825	1·000
Targeted treatment	0·56 (0·30–1·01)	0·058	0·525

Kuderer, *et al.. Lancet.* 20 June 2020;395:1907-1918. Lee, *et al.. Lancet.* 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 15

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)



UK Coronavirus Cancer Monitoring Project (UKCCMP)

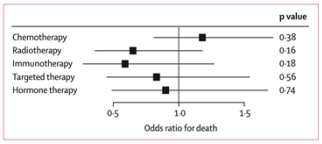


Figure 4: **Forest plots showing effect of anticancer treatments and mortality from COVID-19**
Odds ratios were adjusted for age, gender, and comorbidities. Whiskers indicated 95% CI.

Kuderer, *et al.*. *Lancet.* 20 June 2020;395:1907-1918. Lee, *et al.*. *Lancet.* 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 16

What happens when you have cancer and get COVID-19?

COVID-19 and Cancer Consortium (CC19)

CONCLUSION:

Active Cancer = bad prognosis

Cancer Rx <4wks = OK

UK Coronavirus Cancer Monitoring Project (UKCCMP)

CONCLUSION:

Active Cancer = OK

Cancer Rx <4wks = OK

Kuderer, *et al.*. *Lancet.* 20 June 2020;395:1907-1918. Lee, *et al.*. *Lancet.* 20 June 2020;395:1919-1926.

GW ONCOLOGY UPDATE 17

What happens when you have cancer and get COVID-19?

Journal of Clinical Oncology

Outcomes of COVID-19 in Patients With Cance Report From the National COVID Cohort Collaborative (N3C)

Noha Sharafeldin, MD, PhD, MSc[1]; Benjamin Bates, MD[2]; Qianqian Song, PhD[3]; Vithal Madhira, MS[4]; Yao Yan, BS[3,4]; Sharlene Dong, MS[3]; Eileen Lee, BSE[4]; Nathaniel Kuhrt, BS[3]; Yu Raymond Shao, MD, PhD[3]; Feifan Liu, PhD[5]; Timothy Bergquist, PhD[6]; Justin Guinney, PhD[3]; Jing Su, PhD[3]; and Umit Topaloglu, PhD[4]; on behalf of the National COVID Cohort Collaborative

Cohort study
Jan 2020 – Mar 2021
50 US medical centers; age 18-90+
Cancer patients (n = 398,579) of which 15.9% with new dx COVID-19+ (n = 63,413)
Assessed all-cause mortality

Sharafeldin, *et al.*. *J Clin Oncol.* 4 June 2021;39(20):2232-2246.

GW ONCOLOGY UPDATE 18

What happens when you have cancer and get COVID-19?

National COVID Cohort Collaborative (N3C)

TABLE 1. Study Cohort Demographic, Clinical, and Tumor Characteristics

Baseline Characteristic	Total (N = 373,780), No. (%)	COVID-19–Positive (n = 38,614), No. (%)
Type of primary malignancy[a]		
Skin cancers	51,778 (13.85)	5,743 (14.87)
Breast cancer	51,018 (13.65)	5,482 (14.20)
Prostate cancer	39,472 (10.56)	4,738 (12.27)
Hematologic cancers	39,345 (10.53)	4,749 (12.30)
GI cancers	37,543 (10.04)	3,413 (8.84)
Multisite	52,443 (14.03)	4,225 (10.94)
Type of cancer therapy (yes)[f]		
Cytotoxic	5,193 (1.39)	333 (0.86)
Targeted	3,895 (1.04)	324 (0.84)
Immunotherapy	1,753 (0.46)	147 (0.38)
Endocrine	3,225 (0.86)	259 (0.67)

Sharafeldin, *et al*.. *J Clin Oncol*. 4 June 2021;39(20):2232-2246.

GW ONCOLOGY UPDATE 19

What happens when you have cancer and get COVID-19?

National COVID Cohort Collaborative (N3C)

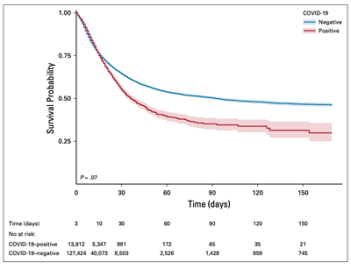


FIG 2. Survival probability curves for COVID-19–positive and COVID-19–negative patients.

Sharafeldin, *et al*.. *J Clin Oncol*. 4 June 2021;39(20):2232-2246.

GW ONCOLOGY UPDATE 20

What happens when you have cancer and get COVID-19?

National COVID Cohort Collaborative (N3C)

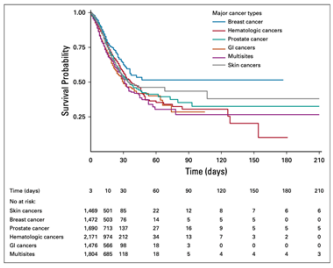


FIG 3. Survival probability curve by cancer type for COVID-19–positive patients.

Sharafeldin, *et al*.. *J Clin Oncol*. 4 June 2021;39(20):2232-2246.

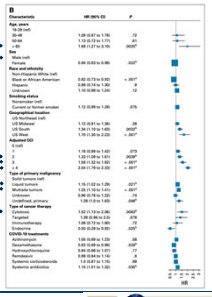
GW ONCOLOGY UPDATE 21

What happens when you have cancer and get COVID-19?

National COVID Cohort Collaborative (N3C)

FIG 4. Adjusted HRs Cox proportional hazard model for association of potential risk factors with 1-year all-cause mortality in (A) entire cohort, and (B) COVID-19–positive patients only. CCI, Charlson Comorbidity Index; HR, hazard ratio; ref, reference. [a]*P* < .001. [b]*P* < .05. (continued on following page)

Characteristic	HR (95% CI)	*P*
Type of cancer therapy		
Cytotoxic	1.52 (1.13 to 2.06)	.0063[b]
Targeted	1.39 (0.96 to 2.0)	.078
Immunotherapy	1.08 (0.72 to 1.60)	.72
Endocrine	0.50 (0.28 to 0.92)	.025[b]



Sharafeldin, *et al.*. *J Clin Oncol.* 4 June 2021;39(20):2232-2246.

GW ONCOLOGY UPDATE 22

What happens when you have cancer and get COVID-19?

National COVID Cohort Collaborative (N3C)

Characteristic	HR (95% CI)	*P*
Type of cancer therapy		
Cytotoxic	1.52 (1.13 to 2.06)	.0063[b]
Targeted	1.39 (0.96 to 2.0)	.078
Immunotherapy	1.08 (0.72 to 1.60)	.72
Endocrine	0.50 (0.28 to 0.92)	.025[b]

CONCLUSION:

Chemotherapy <4wks = bad

Sharafeldin, *et al.*. *J Clin Oncol.* 4 June 2021;39(20):2232-2246.

GW ONCOLOGY UPDATE 23

Hematopoietic stem-cell transplant COVID-19⁺ patients do poorly

Clinical characteristics and outcomes of COVID-19 in haematopoietic stem-cell transplantation recipients: an observational cohort study

Akshay Sharma*, Neel S Bhatt*, Andrew St Martin, Muhammad Bilal Abid, Jenni Bloomquist, Roy F Chemaly, Christopher Dandoy, Jordan Gauthier, Lohith Gowda, Miguel-Angel Perales, Stuart Seropian, Bronwen E Shaw, Eileen E Tuschl, Amer M Zeidan, Marcie L Riches†, Gunjan L Shah†

Retrospective CIBMTR registry study (Mar 2020 – Aug 2021)

HSCT recipients new dx COVID-19⁺ (n = 318).

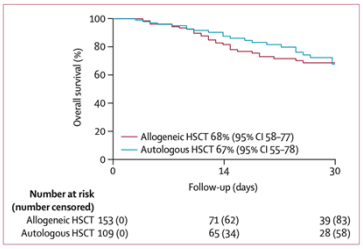
Median time from HSCT:
allogeneic 17 mos. (range 8-46)
autologous 23 mos. (range 8-51)

Assessed 30-day all-cause mortality.

Sharma, *et al.*. *Lancet Haematol.* Mar 2021;8(3):e185-e193.

GW ONCOLOGY UPDATE 24

Hematopoietic stem-cell transplant COVID-19⁺ patients do poorly



Number at risk (number censored)		
Allogeneic HSCT 153 (0)	71 (62)	39 (83)
Autologous HSCT 109 (0)	65 (34)	28 (58)

(vs. 49% mild COVID-19 disease severity)

Figure: Overall survival after COVID-19 diagnosis

Sharma, *et al.*. *Lancet Haematol*. Mar 2021;8(3):e185-e193.

GW ONCOLOGY UPDATE 25

Hematopoietic stem-cell transplant COVID-19⁺ patients do poorly

Table 4: Multivariable analysis for risk factors associated with death from COVID-19

	Number events/ evaluable	Hazard ratio (95% CI)	p value
Allogeneic HSCT			
Age, years			
<50	10/84	1·00	NA
≥50	26/66	2·53 (1·16–5·52)	0·020
Sex			
Female	7/64	1·00	NA
Male	19/86	3·53 (1·44–8·67)	0·006
Time from HSCT to COVID-19, months			
>12	15/96	1·00	NA
≤12	11/54	2·67 (1·33–5·36)	0·005
Race			
White	21/121	1·00	0·74
African American, Asian, Pacific Islander, Native American, or more than one race	3/16	1·52 (0·45–5·06)	0·49
Not reported	2/16	1·95 (0·31–12·04)	0·48
Ethnicity			
Not Hispanic or Latino	24/92	1·00	0·62
Hispanic or Latino	5/28	0·67 (0·23–1·99)	0·47
Non-US resident or ethnicity not reported	2/23	1·24 (0·59–3·08)	0·64
HCT-CI score pre-transplantation			
0–2	19/86	1·00	0·26
≥3	16/60	1·81 (0·89–3·69)	0·11
Not reported	2/7	1·70 (0·20–14·52)	0·63
Immunosuppression within 6 months before COVID-19			
No	21/107	1·00	0·45
Yes	13/79	1·55 (0·74–3·26)	0·24
Not reported	2/17	0·77 (0·18–3·38)	0·73
Autologous HSCT			
Age, years			
<50	2/25	1·00	NA
≥50	22/78	3·31 (0·77–14·19)	0·11
Sex			
Female	8/41	1·00	NA
Male	16/62	1·90 (0·80–4·51)	0·14
Time from HSCT to COVID-19, months			
>12	15/69	1·00	NA
≤12	9/34	0·54 (0·23–1·22)	0·88
Race			
White	12/58	1·00	0·47
African American, Asian, Pacific islander, Native American, or more than one race	5/32	0·60 (0·21–1·67)	0·33
Not reported	2/13	0·51 (0·13–2·04)	0·38
Ethnicity			
Not Hispanic or Latino	13/69	1·00	0·53
Hispanic or Latino	2/23	1·28 (0·48–3·42)	0·62
Non-US resident or ethnicity not reported	4/11	1·93 (0·65–5·64)	0·24
HCT-CI score pre-transplantation			
0–2	9/45	1·00	0·34
≥3	13/55	1·67 (0·81–3·54)	0·88
Not reported	2/2	3·25 (0·66–15·95)	0·15
Disease for HSCT			
Plasma cell disorder or myeloma	12/69	1·00	NA
Lymphoma	12/34	2·41 (1·08–5·38)	0·033

(Table 4 continues on next page)

HSCT=haematopoietic stem cell transplantation. HCT-CI=haematopoietic cell transplantation specific comorbidity index. NA=not applicable.

Table 4: Multivariable analysis for risk factors associated with death from COVID-19

Sharma, *et al.*. *Lancet Haematol*. Mar 2021;8(3):e185-e193.

GW ONCOLOGY UPDATE 26

CLL with COVID-19⁺ do poorly; but does ibrutinib help?

ARTICLE

Chronic lymphocytic leukemia

COVID-19 severity and mortality in patients with chronic lymphocytic leukemia: a joint study by ERIC, the European Research Initiative on CLL, and CLL Campus

Lydia Scarfò[1] · Thomas Chatzikonstantinou[2] · Gian Matteo Rigolin[3] · Giulia Quaresmini[3] · Marina Motta[3] · Candida Vitale[4] · Jose Antonio Garcia-Marco[5,6] · José Ángel Hernández-Rivas[7,8] · Fatima Mirás[9] · Mónica Bailo[10] · Juan Manquez[11] · Carsten U. Niemann[12,13] · Gianluigi Reda[14] · Talha Munir[15,16] · Eva Gimeno[17] · Monia Marchetti[18,19] · Francesca Maria Quaglia[20] · Marzia Varettoni[21] · Julio Delgado[22] · Sunil Iyengar[23] · Ann Janssens[24] · Roberto Marasca[25] · Angela Ferrari[26] · Carolina Cuéllar-García[27,28] · Gilad Itchaki[29] · Martin Špaček[30] · Lorenzo De Paoli[31] · Luca Laurenti[32] · Mark-David Levin[33] · Enrico Lista[34] · Francesco R. Mauro[35] · Martin Šimković[36] · Ellen Van Der Spek[37] · Elisabeth Vandenberghe[38] · Livio Trentin[39,40] · Ewa Wasik-Szczepanek[41] · Rosa Ruchlemer[42] · Dominique Bron[43] · Maria Rosaria De Paolis[44] · Giovanni Del Poeta[45] · Lucia Farina[46] · Myriam Foglietta[47] · Massimo Gentile[48] · Yair Herishanu[49] · Tobias Herold[50,51] · Oren Jakis[49] · Arnon P. Kater[52] · Sabina Kersting[53] · Lara Maletta[54] · Loredia Orsucci[55] · Viola Maria Popov[56,57] · Paolo Sportoletti[58,59] · Mohamed Yassin[60] · Barbara Pocali[61] · Gabor Barna[62] · Annalisa Chiarenza[63] · Gimena dos Santos[64,65] · Eugene Nikitin[66] · Martin Andres[67,68] · Maria Dimou[69,70] · Michael Doubek[71,72] · Alicia Enrico[73] · Yervand Hakobyan[74] · Olga Kalashnikova[75] · Macarena Ortiz Pareja[76] · Maria Papaioannou[77] · Davide Rossi[78,79] · Nimish Shah[80] · Amit Shrestha[81] · Oana Stanciu[82] · Niki Stamatopoulos[83] · Vladimir Strugov[84] · Constantine Tam[85,86] · Mihwa Zdrenghea[87] · Marta Coscia[3] · Kostas Stamatopoulos[88] · Giuseppe Rossi[1] · Alessandro Rambaldi[89,90] · Emili Montserrat[91] · Robin Foà[92] · Antonio Cuneo[3] · Paolo Ghia[93]

Cohort study

Mar 2020 – May 2020

European study; age 48-94

CLL patients with new dx COVID-19⁺ (n = 190)

Assessed mortality / severe disease

Scarfo, *et al.*. *Leukemia*. 34:2354-2363. Published online 9 July 2020.

GW ONCOLOGY UPDATE 27

CLL with COVID-19+ do poorly; but does ibrutinib help?

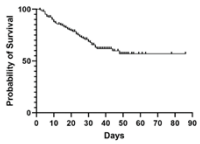


Fig. 1 Overall survival in our patient cohort ($n = 190$). Overall survival of patients with CLL and COVID-19 in days from suspected COVID-19 until last follow-up.

median OS not reached;
69% of patients alive at 30 days

Scarfo, *et al.*. *Leukemia*. 34:2354-2363. Published online 9 July 2020.

GW ONCOLOGY UPDATE 28

CLL with COVID-19+ do poorly; but does ibrutinib help?

Table 3 Patients' disposition based on COVID-19 severity.

Variable	Severe COVID-19 ($n = 151$)	Nonsevere COVID-19 ($n = 39$)	p
Age			
≥65 years (%)	112 (74.2)	17 (43.6)	**<0.05**
<65 years (%)	39 (25.8)	22 (56.4)	
Treatment for CLL			
Untreated (%)	64 (42.7)	9 (23.1)	**<0.05**
Treated (%)	86 (57.3)	30 (76.9)	
Treatment during the last 12 months or ongoing			
Yes (%)	60 (39.7)	24 (61.5)	**<0.05**
Untreated or treated > 12 months before (%)	91 (60.3)	15 (38.5)	

Hospitalization rate for severe COVID-19 was lower for those on ibrutinib (OR 0.44 [95% CI 0.20–0.96] $p < 0.05$) as compared to those receiving any other CLL-specific treatment or off treatment.

Table 1 Patients' characteristics.

Characteristic	Result
On treatment at the time of COVID-19 (%)	65 (34.2%)
BTK inhibitor (acalabrutinib, ibrutinib, zanubrutinib) (%)	44 (67.7)
Venetoclax-based regimens (%)	9 (13.8)
Idelalisib (%)	3 (4.6)
Chlorambucil ± obinutuzumab (%)	3 (4.6)
Bendamustine + rituximab (%)	2 (3.1)
Other (chemotherapy ± steroids) (%)	4 (6.2%)

Scarfo, *et al.*. *Leukemia*. 34:2354-2363. Published online 9 July 2020.

GW ONCOLOGY UPDATE 29

Convalescent plasma

U.S. FOOD & DRUG ADMINISTRATION

February 4, 2021

FDA In Brief: FDA Updates Emergency Use Authorization for COVID-19 Convalescent Plasma to Reflect New Data

Today, the FDA is revising the Letter of Authorization for COVID-19 convalescent plasma to limit the authorization to the use of high titer COVID-19 convalescent plasma only for the treatment of

Hospitalized patients with COVID-19:

- early in the disease course
- who have impaired humoral immunity
- who cannot produce an adequate antibody response.

Plasma with low levels of antibodies has not been shown to be helpful in COVID-19.

GW ONCOLOGY UPDATE 30

Convalescent plasma therapy in patients with a hematologic malignancy hospitalized for COVID-19 (June 2021)

RECOMMENDATION: convalescent plasma for patients with a hematologic malignancy hospitalized for COVID-19 and who lack access to SARS-CoV-2 monoclonal Ab.

JAMA Oncology | Original Investigation

Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19

Michael A. Thompson, MD, PhD; Jeffrey P. Henderson, MD, PhD; Pankil K. Shah, MD, MSPH; Samuel M. Rubinstein, MD; Michael J. Joyner, MD; Toni K. Choueiri, MD; Daniel B. Flora, MD, PharmD; Elizabeth A. Griffiths, MD; Anthony P. Gulati, MD; Clara Hwang, MD; Vadim S. Koshkin, MD; Esperanza B. Papadopoulos, MD; Elizabeth V. Robilotti, MD, MPH; Christopher T. Su, MD, MPH; Elizabeth M. Wulff-Burchfield, MD; Zhuoer Xie, MD, MS; Peter Paul Yu, MD; Sanjay Mishra, MS, PhD; Jonathon W. Senefeld, PhD; Dimpy P. Shah, MD, PhD; Jeremy L. Warner, MD, MS; for the COVID-19 and Cancer Consortium

Retrospective registry study (Mar 2020 – Jan 2021)

Hematologic malignancy patients hospitalized COVID-19+

Improved 30-day all-cause mortality in those received convalescent plasma (n=143) vs. did not (n=823)

HR = 0.60 (95% CI, 0.37-0.97).

Table 3. Association Between Convalescent Plasma Use and Death Within the Crude Analysis, Multivariable Analysis, and Propensity Score Analyses

Variable	HR (95% CI) for death within 30 days
Overall population	
No. of events/No. of patients at risk (%)	223/966 (23.1)
Convalescent plasma	19/143 (13.3)
No convalescent plasma	204/823 (24.8)
Crude analysis[a]	0.47 (0.30-0.76)
Multivariable analysis[b]	0.60 (0.37-0.97)
Propensity score matching[c]	0.52 (0.29-0.92)
Subgroup requiring ICU admission	
No. of events/No. of patients at risk (%)	135/338 (39.9)
Convalescent plasma	12/76 (15.8)
No convalescent plasma	123/262 (46.9)
Crude analysis[a]	0.26 (0.14-0.47)
Multivariable analysis[b]	0.30 (0.16-0.56)
Propensity score matching[c]	0.40 (0.20-0.80)
Subgroup requiring mechanical ventilatory support	
No. of events/No. of patients at risk (%)	105/227 (46.3)
Convalescent plasma	8/45 (17.8)
No convalescent plasma	97/182 (53.3)
Crude analysis[a]	0.24 (0.16-0.49)
Multivariable analysis[b]	0.23 (0.10-0.50)
Propensity score matching[c]	0.32 (0.14-0.72)

Thompson, *et al.*. *JAMA Oncol.* 17 Jun 2021; Online ahead of print.

GW ONCOLOGY UPDATE 31

Monoclonal Ab

U.S. FOOD & DRUG ADMINISTRATION

November 09, 2020

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19

Today, the U.S. Food and Drug Administration issued an emergency use authorization (EUA) for the investigational monoclonal antibody therapy bamlanivimab for the treatment of mild-to-moderate COVID-19 in adult and pediatric patients. Bamlanivimab is authorized for patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kilograms (about 88 pounds), and who are at high risk for progressing to severe COVID-19 and/or hospitalization. This includes those who are 65 years of age or older, or who have certain chronic medical conditions.

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful antigens such as viruses. Bamlanivimab is a monoclonal antibody that is specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells.

GW ONCOLOGY UPDATE 32

Monoclonal Ab

U.S. FOOD & DRUG ADMINISTRATION

November 09, 2020

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19

Bamlanivimab is not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. A benefit of bamlanivimab treatment has not been shown in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

GW ONCOLOGY UPDATE 33

Q: Continue cancer therapy in COVID-19+?

Anti-cancer Therapy for Patients with COVID-19 Infection: Should cancer therapy be delayed in patients who are infected with COVID-19?

"Until more definitive information emerges, decisions about interrupting anti-cancer treatment in patients with active COVID-19 should be based on a clinical benefit:risk assessment that considers the risk of interrupting cancer treatment versus the still poorly defined risk of adverse COVID-19 outcomes in patients receiving active cancer treatment."

ASCO

https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/cancer-treatment-supportive-care

Q: Cancer therapy in COVID-19+: Drug-Drug Interactions

Hot Topic

Cancer, immune suppression and Coronavirus Disease-19 (COVID-19): Need to manage drug safety (French Society for Oncology Pharmacy [SFPO] guidelines)☆

Cancer Treatment Reviews 88 (2020) 102063

Florian Slimano[a,b,*], Amandine Baudouin[c,1], Jérémie Zerbit[d,1], Anne Toulemonde-Deldicque[e,1], Audrey Thomas-Schoemann[c,f,1], Régine Chevrier[g], Mikaël Daouphars[h], Isabelle Madelaine[i], Bertrand Pourroy[j], Jean-François Tournamille[k], Alain Astier[l], Florence Ranchon[c,o], Jean-Louis Cazin[m,n,1], Christophe Bardin[d,1], Catherine Rioufol[c,o]

https://pubmed.ncbi.nlm.nih.gov/32623296/

Q: Surgery for Cancer in COVID-19+?

Surgery: Can/should surgery be canceled or delayed? If surgery is delayed, should patients be started earlier on neoadjuvant therapy if that is an available option?

"Clinicians and patients will need to make individual determinations based on the potential harms of delaying needed cancer-related surgery…
Also, if the surgery requires post-operative intensive care, the current capacity of the intensive care units available for that care should be considered as part of decision making.."

"In some situations (e.g. early-stage breast cancer) where neoadjuvant therapy is available but not routinely considered, it may be reasonable to consider neoadjuvant therapy instead of surgery or simply delaying surgery... However, neoadjuvant therapy that requires clinic visits and clinician-patient contact or that itself is immunosuppressive is associated with risks to the patient that must also be considered."

ASCO

https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/cancer-treatment-supportive-care

Q: Radiation Therapy for cancer in COVID-19⁺?

Radiation: Can/should the initiation of radiation be delayed? Can radiation be interrupted or postponed if already in progress?

"ASCO encourages clinicians to follow ASTRO's current guidance…"

"if hypofractionated schedules are considered clinically acceptable, they should be considered…"

"patients receiving radiation for symptom control or at low risk of harm due to alteration of schedule for radiation treatment visits could potentially be safely delayed…"

ASCO

https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/cancer-treatment-supportive-care

GW ONCOLOGY UPDATE 37

Q: Continue Immune Check-Point Inhibitors in COVID-19⁺?

Immune Checkpoint Inhibitors: Can/should treatment with immune checkpoint inhibitors (e.g. ipilimumab, nivolumab) be delayed or interrupted? Are any special precautions or actions needed with respect to their use?

EUROPEAN SOCIETY OF CLINICAL ONCOLOGY RECOMMENDS INTERRUPTION OF ICI THERAPY IF COVID-19⁺.

ESMO

"There are mixed data regarding the impact of immune checkpoint inhibitors (ICI) on COVID-19 infection in patients with cancer…"

"These agents may cause immune-related serious adverse events and immunosuppression may be necessary as a treatment for those events. The potential harms and benefits of therapy should be carefully considered for each patient…"

"It may be appropriate to adjust to less frequent dosing intervals when different schedules are considered reasonable options."

ASCO

https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/cancer-treatment-supportive-care

GW ONCOLOGY UPDATE 38

Additional Points: Resuming Cancer therapy: follow as below.

CDC

Symptom-Based Strategy for Discontinuing Transmission-Based Precautions

Patients with mild to moderate illness who are *not* severely immunocompromised:

- At least 10 days have passed *since symptoms first appeared* **and**
- At least 24 hours have passed *since last* fever without the use of fever-reducing medications **and**
- Symptoms (e.g., cough, shortness of breath) have improved

Patients who were asymptomatic throughout their infection and are *not* severely immunocompromised:

- At least 10 days have passed since the date of their first positive viral diagnostic test.

Patients with severe to critical illness or who are severely immunocompromised:

- At least 10 days and up to 20 days have passed *since symptoms first appeared* **and**
- At least 24 hours have passed *since last* fever without the use of fever-reducing medications **and**
- Symptoms (e.g., cough, shortness of breath) have improved
- Consider consultation with infection control experts

Patients who are **severely immunocompromised** may produce replication-competent virus beyond 20 days after symptom onset or, for those who were asymptomatic throughout their infection, the date of their first positive viral test. Consultation with infectious diseases specialists is recommended. Use of a test-based strategy for determining when Transmission-Based Precautions may be discontinued could be considered.

GW ONCOLOGY UPDATE 39

Capacity to form anti-COVID-19 Abs is reduced in CLL

LETTER

Chronic lymphocytic leukemia

Anti-SARS-CoV-2 antibody response in patients with chronic lymphocytic leukemia

Lindsey E. Roeker[1] · David A. Knorr[1] · Melissa S. Pessin[2] · Lakshmi V. Ramanathan[2] · Meghan C. Thompson[1] · Lori A. Leslie[3] · Andrew D. Zelenetz[4] · Anthony R. Mato[1]

21 CLL patients: COVID-19+ by nasopharyngeal pcr.
at median 55 days (28-93),

67% pos SARS-CoV-2 Ab.
33% neg SARS-CoV-2 Ab.

Hypogammaglobulinemia was negatively assoc with development anti-SARS-CoV-2 IgG (OR 0.05, 95% CI 0.003–0.7, p= 0.027) .

Currently receiving CLL-directed therapy (OR 0.2, 95% CI 0.03–1.5, p = 0.11) including BTKi use (OR 0.1, 95% CI 0.008–1.3, p = 0.08) were not.

Roeker, *et al. Leukemia*. Nov 2020;34:3047-3049. Published online 27 Aug 2020.

NEWS RELEASE

August 12, 2021

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals

Other fully vaccinated individuals do not need an additional vaccine dose right now

Today, the U.S. Food and Drug Administration amended the emergency use authorizations (EUAs) for both the Pfizer-BioNTech COVID-19 Vaccine and the Moderna COVID-19 Vaccine to allow for the use of an additional dose in certain immunocompromised individuals, specifically, solid organ transplant recipients or those who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices is scheduled to meet Friday to discuss further clinical recommendations regarding immunocompromised individuals. Today's action does not apply to people who are not immunocompromised.

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised?utm_medium=email&utm_source=govdelivery

NEWS RELEASE

August 12, 2021

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals

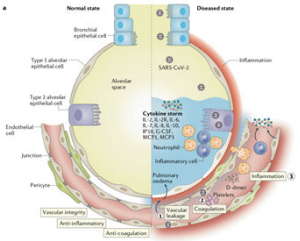
Other fully vaccinated individuals do not need an additional vaccine dose right now

It is recommended that immunocompromised individuals discuss monoclonal antibody treatment options with their health care provider should they contract or be exposed to COVID-19. The FDA has authorized monoclonal antibody treatments for emergency use during this public health emergency for adults and pediatric patients (ages 12 and older weighing at least 40 kilograms or about 88 pounds) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. One authorized product includes use for preventative (prophylaxis) treatment after being exposed to SARS-CoV-2; however, this product is not a substitute for vaccination.

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised?utm_medium=email&utm_source=govdelivery

Hypercoagulabiity of COVID-19

COVID-19 = highly inflammatory/coagulopathic clinicopathologic state.



Teuwen, *et al. Nat Rev Immunol.* 2020;20(7):389-391.

GW ONCOLOGY UPDATE 43

Hypercoagulabiity of COVID-19

ORIGINAL ARTICLE

Risk of venous thromboembolism in patients with COVID-19: A systematic review and meta-analysis

Stephan Nopp MD[1] | Florian Moik MD[1] | Bernd Jilma MD[2] | Ingrid Pabinger MD[1] | Cihan Ay MD[1,3]

[1] Clinical Division of Haematology and Haemostaseology, Department of Medicine I, Medical University of Vienna, Vienna, Austria
[2] Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria
[3] I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia

rpth research & practice in thrombosis & haemostasis

Nopp, *et al. Res Pract Thromb Haemost.* 2020;4:1178-1191.

GW ONCOLOGY UPDATE 44

Hypercoagulabiity of COVID-19

TABLE 3 Prevalence of venous thromboembolism, pulmonary embolism and deep vein thrombosis in ICU and non-ICU hospitalized patients with COVID-19

Outcome	Studies	Number of patients	Number of outcomes	Estimate of prevalence, % (95%CI)	Heterogeneity (I^2)
ICU patients only					
VTE (studies reporting both outcomes)	25	2966	417	22.7 (18.1-27.6)	87.3
No Screening	20	2791	335	18.7 (14.9-22.9)	83.1
Screening[a]	5	175	82	45.6 (30.6-61.1)	73.4
PE (±DVT)[b]	27	3085	410	13.7 (10.0-17.9)	87.6
DVT (±PE)	28	3001	423	18.7 (12.6-25.6)	94.6
No Screening	19	2642	251	8.9 (5.9-12.4)	86.2
Screening[a]	9	359	172	48.1 (35.0-66.2)	91.0
Non-ICU hospitalized patients[c]					
VTE (studies reporting both outcomes)	23	7390	411	7.9 (5.1-11.2)	94.6
No Screening	19	7053	321	5.5 (3.4-7.9)	91.0
Screening[a]	4	337	90	23.0 (3.2-52.9)	96.5
PE (±DVT)[b]	23	8498	263	3.5 (2.3-5.1)	88.9
DVT (±PE)	22	10 519	256	4.1 (2.3-6.4)	94.6
No Screening	14	9835	144	1.4 (0.7-2.3)	85.0
Screening[a]	8	684	112	12.7 (3.7-25.1)	94.1

Note: The meta-analysis of VTE comprises all studies reporting rates of PE and DVT, the analysis of PE comprises all studies reporting PE as a separate outcome and the analysis of DVT comprises studies reporting DVT rates separately. Studies with a suspected high risk of bias have been excluded from these analyses.
Abbreviations: DVT, deep vein thrombosis; ICU, intensive care unit; PE, pulmonary embolism; VTE, venous thromboembolism.
[a]In one study screening was performed in 28% of total patients (ICU, 53%; non-ICU hospitalized, 14%).[17]
[b]No screening for pulmonary embolism was performed.
[c]All patients who were hospitalized at study baseline, excluding ICU patients. ICU admission during later hospital course was possible.

Nopp, *et al. Res Pract Thromb Haemost.* 2020;4:1178-1191.

GW ONCOLOGY UPDATE 45

Hypercoagulabiity of COVID-19

66 studies (28,173 patients) included.

Overall VTE prevalence = 14.1% with ultrasound screening
= 9.5% without screening.

VTE prevalence = 7.9% in non-ICU
= 22.7% in ICU patients.

PE prevalence = 3.5% in non-ICU
= 13.7% ICU patients.

Teuwen, *et al. Nat Rev Immunol.* 2020;20(7):389-391.

GW ONCOLOGY UPDATE 46

Hypercoagulabiity of COVID-19

Association of Treatment Dose Anticoagulation With In-Hospital Survival Among Hospitalized Patients With COVID-19

Ishan Paranjpe, BS
Valentin Fuster, MD, PhD
Anuradha Lala, MD
Adam J. Russak, MD
Benjamin S. Glicksberg, PhD
Matthew A. Levin, MD
Alexander W. Charney, MD, PhD
Jagat Narula, MD, PhD
Zahi A. Fayad, PhD
Emilia Bagiella, PhD
Shan Zhao, MD, PhD
Girish N. Nadkarni, MD, MPH

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
JACC

n = 2,773

Single-institution retrospective study hospitalized pats: examine effect of full-dose AC.

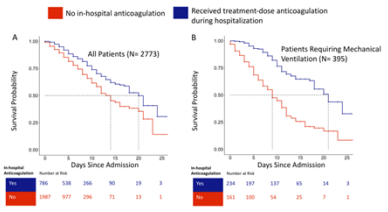
Compared:
ANY treatment-dose systemic AC (28% pats, median 3 days duration, any reason)
vs.
NO treatment-dose systemic AC.

Paranjpe, *et al. J Am Coll Cardiol.* 7 Jul 2020;76(1):122-124.

GW ONCOLOGY UPDATE 47

Hypercoagulabiity of COVID-19

In-hospital mortality for patients treated with AC: 22.5% with a median survival of 21 days, compared to 22.8% and median survival of 14 days in patients who did not receive AC.



In patients who required mechanical ventilation (N=395), in-hospital **mortality was 29.1%** with a median survival of 21 days for those treated **with AC** as compared to **62.7%** with a median survival of 9 days in patients who did **not receive AC**.

Paranjpe, *et al. J Am Coll Cardiol.* 7 Jul 2020;76(1):122-124.

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Hypercoagulabiity of COVID-19

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19

The REMAP-CAP, ACTIV-4a, and ATTACC Investigators*

"We conducted an international, adaptive, multi-platform, randomized, controlled trial to determine whether an initial strategy of therapeutic-dose anticoagulation with unfractionated or low-molecular-weight heparin improves in-hospital survival and reduces the duration of intensive care unit (ICU)–level cardiovascular or respiratory organ support in critically ill patients with Covid-19. "

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

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"We conducted an international, adaptive, multiplatform, randomized, controlled trial to determine whether an initial strategy of therapeutic- dose anticoagulation with unfractionated or low-molecular-weight heparin improves in hospital survival and reduces the duration of ICU- level cardiovascular or respiratory organ support among hospitalized patients with Covid-19 who are not critically ill.

REMAP-CAP Investigators *et al. NEJM.* 4 Aug 2021;published Online.
ATTACC Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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Therapeutic-dose anticoagulation was administered for up to 14 days or until recovery

Usual-care thromboprophylaxis was administered at a dose and duration determined by the treating clinician according to local practice, which included either standard low-dose thromboprophylaxis or enhanced intermediate-dose thromboprophylaxis.

The primary outcome, organ support–free days, was evaluated… up to day 21 among patients who survived

The NEW ENGLAND JOURNAL of MEDICINE

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Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

The ATTACC, ACTIV-4a, and REMAP-CAP Investigators*

REMAP-CAP Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19

The REMAP-CAP, ACTIV-4a, and ATTACC Investigators*

The majority of patients were enrolled through REMAP-CAP (929 of 1103 enrolled patients, 84%)

Among the patients who were assigned to receive usual-care thromboprophylaxis…
standard low- dose thromboprophylaxis in 41% and…
enhanced intermediate-dose thromboprophylaxis in 51%.

The NEW ENGLAND JOURNAL of MEDICINE

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REMAP-CAP Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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The NEW ENGLAND JOURNAL of MEDICINE
ORIGINAL ARTICLE
Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19
The REMAP-CAP, ACTIV-4a, and ATTACC Investigators*

Table 2. Primary and Secondary Outcomes.

Outcome	Therapeutic-Dose Anticoagulation (N=536)	Usual-Care Thromboprophylaxis (N=567)	Adjusted Difference in Risk (95% Credible Interval)	Adjusted Odds Ratio (95% Credible Interval)†	Probability of Superiority	Probability of Futility	Probability of Inferiority
	median no. (IQR)		*percentage points*		%	%	%
Organ support–free days up to day 21†‡	1 (−1 to 16)	4 (−1 to 16)	—	0.83 (0.67 to 1.03)	5.0	99.9	95.0
	no. of patients/total no. (%)						
Survival to hospital discharge‡	335/534 (62.7)	364/564 (64.5)	−4.1 (−10.7 to 2.4)	0.84 (0.64 to 1.11)	10.8	99.6	89.2
Major thrombotic events or death§	213/531 (40.1)	230/560 (41.1)	1.0 (−5.6 to 7.4)	1.04 (0.79 to 1.35)	40.3	—	59.7
Major thrombotic events¶	34/530 (6.4)	58/559 (10.4)	—	—	—	—	—
Death in hospital	199/534 (37.3)	200/564 (35.5)	—	—	—	—	—
Any thrombotic events or death‖	217/531 (40.9)	232/560 (41.4)	1.5 (−4.9 to 8.0)	1.06 (0.81 to 1.38)	33.4	—	66.6
Any thrombotic events‖	38/530 (7.2)	62/559 (11.1)	—	—	—	—	—
Death in hospital	199/534 (37.3)	200/564 (35.5)	—	—	—	—	—
Major bleeding§	20/529 (3.8)	13/562 (2.3)	1.1 (−0.6 to 4.4)	1.48 (0.75 to 3.04)	12.8	—	87.2

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The NEW ENGLAND JOURNAL of MEDICINE
ORIGINAL ARTICLE
Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19
The REMAP-CAP, ACTIV-4a, and ATTACC Investigators*

DISCUSSION

"Our results refute the hypothesis that routine therapeutic-dose anticoagulation benefits critically ill patients with Covid-19.

This hypothesis was based in part on observational studies that reported an association between therapeutic-dose anticoagulation and improved outcomes.

Multiple small and moderate-size randomized trials continue to evaluate different anticoagulation strategies in Covid-19."

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The primary outcome, organ support–free days, was evaluated… up to day 21 among patients who survived

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The ATTACC, ACTIV-4a, and REMAP-CAP Investigators*

Therapeutic-dose anticoagulation was administered for up to 14 days or until recovery

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Hypercoagulabiity of COVID-19


ORIGINAL ARTICLE

Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19

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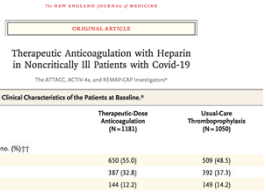
ORIGINAL ARTICLE

Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

The ATTACC, ACTIV-4a, and REMAP-CAP Investigators*

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Therapeutic-Dose Anticoagulation (N = 1181)	Usual-Care Thromboprophylaxis (N = 1050)
Platform of enrollment — no. (%)††		
ATTACC‡‡	650 (55.0)	509 (48.5)
ACTIV-4a	387 (32.8)	392 (37.3)
REMAP-CAP	144 (12.2)	149 (14.2)

Among the 855 patients in the thromboprophylaxis group… 613 (71.7%) received a low dose of a thromboprophylactic drug and 227 (26.5%) received an intermediate dose.

ATTACC Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

The ATTACC, ACTIV-4a, and REMAP-CAP Investigators*

Table 2. Primary Outcome of Organ Support–Free Days.*

Variable	Therapeutic-Dose Anticoagulation	Usual-Care Thromboprophylaxis	Adjusted Difference in Risk (95% Credible Interval)†	Adjusted Odds Ratio (95% Credible Interval)‡	Probability of Superiority of Therapeutic-Dose Anticoagulation
	no. of patients/total no. (%)		*percentage points*		%
Patients with moderate disease					
Overall group§	939/1171 (80.2)	801/1048 (76.4)	4.0 (0.5 to 7.2)	1.27 (1.03–1.58)	98.6
D-dimer cohort¶					
High level	264/339 (77.9)	210/291 (72.2)	5.1 (0.0 to 9.9)	1.31 (1.00–1.76)	97.3
Low level	463/570 (81.2)	403/505 (79.8)	3.0 (−1.2 to 6.3)	1.22 (0.93–1.57)	92.9
Unknown level	212/262 (80.9)	188/252 (74.6)	4.9 (0.00 to 9.9)	1.32 (1.00–1.86)	97.3

ATTACC Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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ORIGINAL ARTICLE

Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

The ATTACC, ACTIV-4a, and REMAP-CAP Investigators*

Table 3. Secondary Outcomes among All Patients with Moderate Disease.*

Outcome	Therapeutic-Dose Anticoagulation	Usual-Care Thromboprophylaxis	Adjusted Difference in Risk (95% Credible Interval)†	Adjusted Odds Ratio (95% Credible Interval)‡	Probability of Effect of Therapeutic-Dose Anticoagulation
	no. of patients/total no. (%)		*percentage points*		%
Survival until hospital discharge	1085/1171 (92.7)	962/1048 (91.8)	1.3 (−1.1 to 3.2)	1.21 (0.87 to 1.68)§	87.1¶
Survival without organ support at 28 days‖	932/1175 (79.3)	789/1046 (75.4)	4.5 (0.9 to 7.7)	1.30 (1.05 to 1.61)	99.1¶
Progression to intubation or death**	129/1181 (10.9)	127/1050 (12.1)	−1.9 (−4.1 to 0.7)	0.82 (0.63 to 1.07)	92.2¶
Major thrombotic event or death	94/1180 (8.0)	104/1046 (9.9)	−2.6 (−4.4 to −0.2)	0.72 (0.53 to 0.98)	98.0¶
Major thrombotic event	13/1180 (1.1)	22/1046 (2.1)			
Death in hospital	86/1180 (7.3)	86/1046 (8.2)			
Major bleeding	22/1180 (1.9)	9/1047 (0.9)	0.7 (−0.1 to 2.3)	1.80 (0.90 to 3.74)	95.5††

ATTACC Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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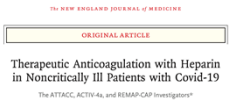
Hypercoagulabiity of COVID-19

DISCUSSION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"On the basis of these findings, for every 1000 hospitalized patients with moderate disease, an initial strategy of therapeutic-dose anticoagulation, as compared with usual-care thromboprophylaxis, would be anticipated to result in the survival of 40 additional patients until hospital discharge without organ support at the expense of 7 additional major bleeding events. Absolute treatment benefits were more apparent in the high d-dimer cohort than in the low d-dimer cohort."

ATTACC Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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Hypercoagulabiity of COVID-19

COVID-19 RESOURCES

AMERICAN SOCIETY OF HEMATOLOGY / COVID-19 RESOURCES / **COVID-19 AND VTE-ANTICOAGULATION**

All hospitalized adults with COVID-19 should receive pharmacologic thromboprophylaxis unless the risk of bleeding outweighs the risk of thrombosis; low-molecular-weight heparin (LMWH) is recommended over unfractionated heparin (UFH) to reduce contact. In the setting of heparin-induced thrombocytopenia, fondaparinux is recommended. Dose adjustment for obesity and renal function may be used per institutional guidance.

Therapeutic- and intermediate-dose anticoagulation are being investigated… in multiple randomized controlled trials (RCT)

For patients requiring ICU level of care:
The ASH guideline panel ***suggests*** using prophylactic-intensity… anticoagulation.

For hospitalized patients not requiring ICU level of care:
The ASH guideline panel ***suggests*** using prophylactic-intensity… anticoagulation.

Should COVID-19 patients receive post-discharge thromboprophylaxis?
The ASH guidelines panel… suggest patients should not receive thromboprophylaxis after hospital discharge for COVID-19 in the absence of other indications.

ATTACC Investigators *et al. NEJM.* 4 Aug 2021;published Online.

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Summary

- Presenting sxs of COVID-19 are the same in cancer patients
- Treatment of COVID-19 is generally same in cancer patients, but consider monoclonal Ab (outpat) and convalescent plasma (hospitalized)
- Having cancer (especially heme, lung, GI) is a risk factor for developing severe COVID-19 infection
- Recent cytotoxic chemotherapy is likely associated with worse outcome COVID-19 (data re: ICI less clear but likely best to hold)
- Consider holding all immunosuppressive therapy with new dx COVID-19+, but targeted therapy (EGFR or BRAF/MEK inhibitors) may be OK
- COVID-19 inflammatory hypercoagulopathy: ASH still recommending standard-dose prophylaxis (not intermediate-dose prophylaxis or therapeutic anti-coagulation) for both ICU and non-ICU hospitalized patients (regardless of cancer status), but further evaluation ongoing

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